UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Information Collection Request (ICR) for the Human Studies Rule
Calculation of Burden and Cost

TO: File

FROM: Kelly Sherman
Human Research Ethics Reviewer
Office of Pesticide Programs

DATE: September 2, 2008

Burden Hours for Respondents

EPA sent consultation questions about the burden and cost estimates to five respondents – the Agricultural Handlers Exposure Task Force (AHETF), the Antimicrobial Exposure Assessment Task Force II (AEATF), Carroll-Loye, ICR, Inc., and Grayson. These five organizations are experienced in submitting human subjects research to OPP, and are expected to make additional submissions over the next several years. The consultation responses received from these respondents indicated that EPA's previous estimates of the burden and cost were too low. To calculate new burden and cost estimates for this renewal ICR, EPA relied upon the estimates provided in the five consultation responses. EPA calculated a weighted average of the different responses, recognizing that some study types are more complicated and costly to conduct than others.

The respondent burden and cost estimates that appear in Table 1 in the ICR, for research involving intentional exposure of human subjects, are the weighted averages of the values in Table A (burden hour estimates for agricultural handler studies, from the AHETF), Table B (burden hour estimates for antimicrobial exposure studies, from the AEATF), and Table C (burden hour estimates for insect repellant studies, averaged from the responses received from Carroll-Loye and ICR, Inc.). The weighted average was calculated by multiplying the burden hour estimates that appear in Tables A, B, and C by

the expected number of each type of study, and then dividing the sum of those products by the total number of studies of all types expected per year. The expected number of studies per year was also determined from the consultation responses.

The respondent burden and cost estimates that appear in Table 2 in the ICR, for all other submitted research with human subjects, are based on the consultation response from Joel Panara at Grayson. Mr. Panara is familiar with submitting completed study reports to EPA for pre-rule research for which HSRB protocol review is not required, and his consultation response was based on his billing records for work performed on several studies to generate the reports necessary to meet the requirements of the rule.

Hourly Rates for Respondents

Four of the five respondents indicated that the hourly rates used by EPA for calculating the estimated costs are too low. In determining the rates, OPP uses a single source of data, the Bureau of Labor Statistics' National Industry-Specific Occupational Employment and Wage Estimates, and selects the appropriate occupational category. Using the BLS data allows EPA to be consistent between across sectors and occupations. If OPP were to separately research wages for each ICR, the methodology in determining the wages would not be consistent and the wage rates could not be compared between sectors and occupations. Some wages would be biased high, while others would be biased low. The BLS wages are categorized by North American Industry Classification System (NAICS) codes, and therefore are industry-specific. They are, however, national averages. Therefore, some of the high wages earned by specialists in high cost localities are offset by others who are less specialized in lower cost localities.

The wage rates used in the draft ICR were from NAICS 325300 (Pesticide, Fertilizer, and Other Agricultural Chemical Manufacturing). Upon reconsidering the possible NAICS categories, EPA has concluded that NAICS 541710 is more appropriate because there are a variety of types of scientists involved in the human studies ICR, with higher education requirements than in pesticide manufacturing companies. The wage rates in NAICS 541710 are slightly higher than those in NAICS 325300, which helps to address the comments in the consultation responses indicating that the hourly rates used by the Agency are too low.

Agency Burden and Costs

The estimated burden and costs to the Agency are derived from input from EPA staff members who have prepared reviews for studies that were presented to the HSRB. Recognizing that some study types are more complicated and time consuming to review that others, EPA calculated a weighted average using the staff time estimates and the expected frequency of receiving different types of studies. The values calculated based on the staff input appear in Tables E, F, and G. The weighted averages are provided in ICR Tables 3 and 4.

Number of Transactions

The estimated number of transactions is based heavily on the consultation responses from the five respondents, as well as EPA's historical experience and knowledge of upcoming submissions.

RESPONDENT BURDEN HOUR ESTIMATES

Table A. Agricultural Handler Exposure Studies – Burden Hour Estimates from AHETF's Consultation Response

Activities	Average Burden Hours Per Occurrence			Total Per Response	
	Management $138	Technical $73	Clerical $42	Hours	Cost ($)
Rule familiarization and training[1]	2	2	2	6	506
Prepare and submit protocol for IRB review[2]	5	80	10	95	6,950
Prepare and submit protocol for EPA and HSRB review[3]	15	240	26	276	20,682
Document ethical conduct of a completed study for which EPA and the HSRB have reviewed the protocol[4]	10	260	10	285	20,780
Store, file, and maintain records[5]	0	2	0	2	48,918

[1] Values taken from table titled "Calculation of IPC per Human Study Based on AHETF Experience" in the AHETF's follow-up consultation response submission, sent via email from David Johnson to Kelly Sherman on 8-15-08.

[2] Values taken from table titled "Calculation of IPC per Human Study Based on AHETF Experience" in the AHETF's follow-up consultation response submission, sent via email from David Johnson to Kelly Sherman on 8-15-08.

[3] Values taken from table titled "Calculation of IPC per Human Study Based on AHETF Experience" in the AHETF's follow-up consultation response submission, sent via email from David Johnson to Kelly Sherman on 8-15-08.

[4] Values taken from table titled "Table 1: Respondent Burden Estimates: Unit Costs of Discrete Activities Required by the New Rule" from the AHETF's original consultation response submission. The AHETF's values, which were provided "per scenario" rather than "per study," were divided by five to obtain per study amounts.

[5] Values taken from table titled "Calculation of IPC per Human Study Based on AHETF Experience" in the AHETF's follow-up consultation response submission, sent via email from David Johnson to Kelly Sherman on 8-15-08.

Table B. Antimicrobial Exposure Studies – Burden Hour Estimates from AEATF's Consultation Response, with the adjustment described in footnote 1

Activities	Average Burden Hours Per Occurrence			Total Per Response	
	Management $138	Technical $73	Clerical $42	Hours	Cost ($)
Rule familiarization and training[6]	2	2	2	6	506
Prepare and submit protocol for IRB review	24	120	40	184	13,752
Prepare and submit protocol for EPA and HSRB review	40	320	40	400	30,560
Document ethical conduct of a completed study for which EPA and the HSRB have reviewed the protocol	24	80	24	148	10,160
Store, file, and maintain records	8	16	16	40	2,944

[6] For the activity "Rule Familiarization and Training," the AEATF estimated 12 management hours, 32 technical hours, and 8 clerical hours, based on expected personnel turnover. Time spent training new staff is not properly attributed to the paperwork and recordkeeping burdens of the rule. This is a one-time activity. Since the AEATF is familiar with the rule, its costs for this activity should be small. Instead of using AEATF's reported numbers, KS used the numbers reported by the AHETF (2 hrs. for each category).

Table C. Insect Repellant Studies – Burden Hour Estimates from an Average of the Consultation Responses from Carroll-Loye and ICR, Inc., with the adjustment described in footnote 2

Activities	Average Burden Hours Per Occurrence			Total Per Response	
	Management $138	Technical $73	Clerical $42	Hours	Cost ($)
Rule familiarization and training[7]	1	1	1	3	253
Prepare and submit protocol for IRB review	54	54	24	132	12,402
Prepare and submit protocol for EPA and HSRB review	20	27	42	89	6,495
Document ethical conduct of a completed study for which EPA and the HSRB have reviewed the protocol	20	42	26	88	6,918
Store, file, and maintain records	3	6	1	10	894

Table D. Documentation of Ethical Conduct of a Completed Study for which EPA and HSRB have NOT reviewed the Protocol (per requirements at §26.1303) – Burden Hour Estimates Based on Consultation Response from Joel Panara at Grayson (a laboratory with experience with submitting this type of info)

Activities	Average Burden Hours Per Occurrence			Total Per Response	
	Management $138	Technical $73	Clerical $42	Hours	Cost ($)
Document ethical conduct of a completed study for which EPA and the HSRB have not reviewed the protocol	5	16	8	29	2,194

[7] For the activity "Rule Familiarization and Training," Carroll-Loye estimated 50 management hours, 100 technical hours, and 10 clerical hours. This is a one-time activity, and since Carroll-Loye is familiar with the rule, its costs for this activity should be small. Thus, instead of using an average of Carroll-Loye's and ICR, Inc.'s numbers, OPP used only the numbers provided by ICR, Inc. for this activity.

For ICR Table 1

Weighted Average Burden and Cost Estimates for Respondents – Research Involving Intentional Exposure of Human Subjects

Activities	Average Burden Hours Per Response			Total Per Response	
	Management $138	Technical $73	Clerical $42	Hours	Cost ($)
Rule familiarization and training[8]	2	4	2	8	652
Prepare and submit protocol for IRB review	31	83	33	147	11,723
Prepare and submit protocol for EPA and HSRB review	25	181	37	243	18,217
Document ethical conduct of a completed study for which EPA and the HSRB have reviewed the protocol	19	113	21	153	11,753
Document ethical conduct of a pre-rule study for which EPA and the HSRB have not reviewed the protocol	5	16	8	29	2,194
Store, file, and maintain records	4	8	6	18	1,388
Total per response	86	405	107	598	45,927

Annual Burden: 598 hours per protocol or completed study * 34 protocols or completed studies per year = 20,332 hours

Annual Costs: $45,927 per study * 34 protocols or completed studies per year = $1,561,518

[8] Comments from the AHETF, AEATF, and ICR, Inc., indicated an average of 2 hours for management, 2 hours for technical, and 2 hours for clerical for the activity "Rule Familiarization and Training." The Agency considers this burden to be representative of the time expenditure by experienced submitters. But EPA recognizes that there may be new inexperienced entities that may need to spend more time on "Rule Familiarization and Training." In order to capture the total burden and cost across all submitters, both experienced and inexperienced, OPP assumed that, in addition to the experienced submitters, there would be one new submitter per year, and that a new submitter would spend 4 management hours, 16 technical hours, and 2 clerical hours on "Rule Familiarization and Training." The weighted average, covering both experienced and inexperienced submitters, is 2 management hours, 4 technical hours, and 2 clerical hours.

For ICR Table 2

Table 2. Respondent Burden and Cost Estimates – All Other Submitted Research with Human Subjects

Activities	Average Burden Hours Per Response			Total Per Response	
	Management $138	Technical $73	Clerical $42	Hours	Cost ($)
Rule familiarization and training	1	1	0	2	211
Prepare and Submit Ethics Information of Completed Human Studies to EPA	0	8	1	9	626
Store, file, and maintain records	0	0	1	1	42
Total per response	1	9	2	12	879

Annual Burden: 12 hours per study * 20 studies submitted per year = 240 hours
Annual Costs: $879 per study * 20 studies submitted per year = $17,580

Agency Burden Hour Estimates: Technical Staff[9]

Table E. Protocol Review

Study Type	Average Annual Number of Protocols	Average Number of Hours Per Protocol Review	Total Number of Hours
AHETF	4	160	640
AEATF	5	120	600
Repellant Efficacy	6	80	480
Other Types of Post-Rule Intentional Exposure Studies	1	80	80
Weighted Average Number of Hours per Protocol Review			**113 hours per protocol**
Estimated Annual Number of Protocol Reviews			**16**

Table F. Review of Completed Studies

Study Type	Average Annual Number of Completed Study Reviews	Average Number of Hours Per Completed Study Review	Total Number of Hours
AHETF	4	80	320
AEATF	5	60	300
Repellant Efficacy	6	40	240
Other Types of Post-Rule Intentional Exposure Studies	1	40	40
Pre-Rule Completed Intentional Exposure Studies that Measure or Identify a Toxic Effect	2	60	120
Weighted Average Number of Hours per Protocol Review			**57 hours per completed study**
Estimated Annual Number of Completed Study Reviews			**18**

Table G. Ethics Reviews for Pre-Rule Completed Studies Not Requiring HSRB Review

Study Type	Average Annual Number of Reviews	Avg. Number of Hours Per Review	Annual Burden Hour Estimate
Pre-Rule completed studies that do NOT measure or identify a toxic effect	**20**	**4**	**80 hours**

[9] Ag handler study estimates based on information from J. Evans, M. Crowley and J. Carley (EPA/OPP). Antimicrobial exposure study estimates based on information from T. Leighton, C. Walls, and J. Carley (EPA/OPP). Insect repellant study estimates based on information from C. Fuentes, K. Sweeney, and J. Carley (EPA/OPP). Other study type estimates based on information from J. Carley, B. Jordan, and K. Sherman.

Burden Hour Estimates: Management and Clerical

Management:

- Assume 2 hours for Protocol Reviews and Completed Study Reviews
- Assume zero hours for Ethics Reviews for studies not requiring HSRB Review

Clerical

- Assume 2 hours for Protocol Reviews and Completed Study Reviews
- Assume 1 hour for Ethics Reviews for studies not requiring HSRB Review

For ICR Table 3

Table 3. Weighted Average Burden and Cost Estimates for Agency – Research Involving Intentional Exposure

Activities	Average Burden Hours Per Response			Total Per Response	
	Management $103	Technical $71	Clerical $41	Hours	Cost ($)
Rule familiarization and training	2	2	0	4	348
Primary Review of Scientific and Ethical Aspects of a Protocol	1	113	0	114	8,126
Primary Review of Ethical Aspects of a Completed Study Report	1	57	0	58	4,150
Secondary Review of Scientific and Ethical Aspects of a Protocol or Review of Ethical Aspects of a Completed Study					4,144*
Store, file, and maintain records	0	0	2	2	82
Total per protocol or completed study	4	172	2	178	16,850

***** Cost of HSRB members working on the HSRB report (collectively spending 240 hours per HSRB report in FY 2008, compensated at the rate of $53/hour), plus the cost of EPA Office of the Science Advisor technical staff working on the HSRB report (171 hours per report, at the technical staff rate of $71/hour). Each HSRB report covers an average of 6 protocols and/or completed studies per report.

Annual Burden: 178 hours per study or protocol * 34 protocols or completed studies = 6,052 hours

Annual Costs: 16,850 * 34 protocols or completed studies = $572,900

Number of Transactions: February 2009 - January 2012

1. **AHETF Monitoring Program**
   - The AHETF monitoring program defines 33 scenarios, each of which will typically involve 5 field studies. About 80 field studies will be needed to complete the program.
   - The AHETF plans to complete the program within 5 years.
   - ~30 scenarios in 5 years = ~ 6 scenarios & 6 protocols per year.
   - For each protocol, there will be a completed study report approximately 1 year later = ~ 6 completed reports per year.
   - Note that approximately 50% of the time, protocols will need to go to the HSRB twice, either because the AHETF chooses to present field studies associated with one scenario at two different HSRB meetings, or because the protocol is not reviewed favorably during the first visit to the HSRB.
   - **Original EPA Estimate (prior to consultation): 6 scenario-specific protocols** and **6 scenario-specific study reports** per year
   - **AHETF Estimate (from consultation): 4 protocols and 4 study reports per year**
   - **Figures used in ICR: 4 protocols and 4 study reports per year, based on AHETF's consultation response**

2. **AEATF Monitoring Program**
   - The AEATF monitoring program defines 17 scenarios, each of which will typically involve a single field study. Some will likely be observational and thus will not need to undergo HSRB review – according to Tim L.
   - The AEATF plans to complete the program within 5 years
   - ~15 scenarios / 5 years = ~ 3 protocols per year.
   - For each protocol, there will be a completed study report, approximately 1 year later = ~ 3 completed reports per year.
   - **Original EPA Estimate (prior to consultation): 3 scenario-specific protocols** and **3 scenario-specific study reports** per year
   - **AEATF Estimate (from consultation): 5 protocols and 5 study reports per year**
   - **Figures used in ICR: 5 protocols and 5 study reports per year, based on AEATF's consultation response**

3. **Insect Repellent Efficacy Testing**
   - For the past two years we have averaged about 3 protocols or completed studies at each HSRB meeting.
   - This is about half the steady-state demand under current requirements.
   - Therefore, ~ 3 protocols per year.
   - For each protocol, there will be a completed study report, approximately 1 year later = ~ 3 completed reports per year.
   - **Original EPA Estimate (prior to consultation): 6 protocols** and **6 completed studies** per year
   - **Carroll-Loye Estimate: an average of 4 protocols and 4 study reports per year**

- **ICR, Inc. Estimate: an average of 2 protocols and 2 study reports per year**
- **Figures used in ICR: 6 protocols and 6 study reports per year, adding together the Carroll-Loye and ICR, Inc. estimates**

4. Other Post-Rule Studies

- These could include exposure studies from sources other than the task forces, ADME studies, skin patch tests of irritation or sensitization, systemic toxicity tests, or others.
- All would require submission of a protocol before execution and of a completed report after execution; both the protocol and the report would require both EPA and HSRB review.
- **Estimate: 1 protocol and 1 completed study per year.** (This is likely an over-estimate)

5. Pre-Rule Completed Studies which measure or identify a toxic effect

- 2 categories:
  - New submissions requiring submission of §26.1303 information
  - Studies retrieved from the literature or from other sources, not subject to §26.1303.
- There is likely to be a steady trickle of these studies – approximately 1 case every-other meeting
- One case may include multiple individual studies with the same chemical
- **Estimate**: **2 cases per year** (requiring study review, but not protocol review)

6. Pre-Rule Completed Studies which do not measure or identify a toxic effect

- These studies do not go to the HSRB, but they do require an EPA ethics review.
- Historical level: 20 reviews per year
- Assume workload to remain constant over the time period of the ICR
- **Estimate: 20 per year** (requiring EPA ethics review only – not HSRB review)

TOTAL TRANSACTIONS PER YEAR:

- **16 protocols** per year requiring EPA & HSRB review
  - AHETF, AEATF, Insect Repellant, and one additional type of post-rule intentional exposure study
- **18 completed study reports** per year requiring EPA & HSRB review
  - 16 completed study reports for which there was previous protocol review
  - 2 pre-rule studies that measure or identify a toxic effect
- **20 studies/year** requiring EPA ethics review, but not HSRB review (pre-rule studies that do not measure or identify a toxic effect)